Butoconazole use in pregnancy: population-based case-control studies on adverse pregnancy outcomes in Hungary (study protocol RGD-77425)

First published: 09/07/2013

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Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/16983

EU PAS number

EUPAS4282

Study ID

16983

DARWIN EU® study

No

Study countries

Hungary

Study status

Finalised

Research institutions and networks

Institutions

Semmelweis University

Hungary

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Institution **Hospital/Clinic/Other health care facility**

Contact details

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 10/07/2013

Actual: 05/07/2013

Study start date
Planned: 10/09/2013

Actual: 20/01/2014

Data analysis start date
Planned: 01/11/2013

Actual: 10/02/2014

Date of final study report
Planned: 30/06/2016

Actual: 21/11/2016

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Gedeon Richter Plc.

Study protocol

Final study protocol RGD77425_20130708.pdf(1.37 MB)

Study protocol RGD77425_Amendment 1_clean_FINAL.pdf(2.22 MB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Data collection methods:

Secondary use of data

Main study objective:

To confirm the results of the F. Rosa study described in (Briggs 2011), i.e. to confirm the lack of teratogenic potential of locally applied butoconazole in humans. In addition, a dedicated case-control analysis is planned on the risk of spontaneous abortion in butoconazole exposed pregnancies. Other gynecologic anti-infectives are also included in these analyses for comparison.

Study Design

Non-interventional study design

Case-control

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name

BUTOCONAZOLE

MICONAZOLE

CLOTRIMAZOLE

NYSTATIN

METRONIDAZOLE

DICLOFENAC

IBUPROFEN

ISOTRETINOIN

VALPROIC ACID

CARBAMAZEPINE

Medical condition to be studied

Congenital anomaly

Abortion spontaneous

Stillbirth

Live birth

Ectopic pregnancy

Low birth weight baby

Pregnancy

Maternal exposure during pregnancy

Population studied

Short description of the study population

All pregnancy outcomes reported to the National Healthcare Fund (OEP) between 01 January 2005 and 31 December 2011 who were exposed to butaconazole.

Age groups

Preterm newborn infants (0 – 27 days)

Term newborn infants (0 – 27 days)

Infants and toddlers (28 days – 23 months)

Children (2 to < 12 years)

Adults (18 to < 46 years)

Special population of interest

Pregnant women

Estimated number of subjects

1100000

Study design details

Outcomes

The study has two co-primary objectives:- to evaluate butoconazole treatment as a potential teratogenic risk factor in a population-based case-control study in Hungary, based on the OEP database,- to evaluate butoconazole treatment as a potential risk factor of spontaneous abortion in a population-based case-control study in Hungary, based on the OEP database. - to evaluate other gynecology anti-infectives (clotrimazole, miconazole, nystatin, metronidazole) as risk factors of teratogenicity or spontaneous abortion for comparative assessment, in the same setting,- to collect epidemiologic data on pregnancy outcomes in butoconazole exposed pregnancies (in compliance with EMEA/CHMP/313666/2005).

Data analysis plan

The planned analyses comprise descriptive statistics of drug exposure in pregnancies with different pregnancy outcomes, analysis of birth weight in unexposed and drug-exposed pregnancies, and case-control studies on spontaneous abortion and congenital abnormalities considering a range of confounding factors and sensitivity analyses. Crude and adjusted odds ratios will be calculated for both of the co-primary outcomes, with several sensitivity analyses and several alternative definitions of relevant drug exposure periods. Results of all these analyses will be evaluated together, to allow for robust conclusions. Any positive finding in these analyses will be interpreted in the context of similar findings with therapeutic comparators.

Documents

Study results

Final Report_20161121_signed_Vol1.pdf(8.21 MB)

Protocol Amendment2_final_clean.pdf(3.09 MB)

Study report

15_1_8.pdf(765.34 KB)

Final Report_20161121_signed_Vol2.pdf(7.59 MB)

Final Report_20161121_signed_Vol3.pdf(7.36 MB)

Study, other information

approval-for-the-clinical-trial-GYEMSZI.pdf(225.99 KB)

butoconazole-nitrate-approval-modification.pdf(120.38 KB)

Final Report_20161121_signed_Vol2.pdf(7.59 MB)

Final Report_20161121_signed_Vol3.pdf(7.36 MB)

Data management

ENCePP Seal

Signed checklist for study protocols

ENCEPP checklist 20150717.pdf(247.37 KB)

Microsoft Word - ENCePP Checklist study RGD77425_20130708.pdf(127.49 KB)

Data sources

Data sources (types)

Administrative healthcare records (e.g., claims)

Other

Data sources (types), other

Prospective patient-based data collection

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No